Gene / Term	Synonyms	Organism
PLK4 polo-like kinase 4	PLK-4, Polo-like kinase 4, Sak, SAK, Serine/threonine-protein kinase 18, Serine/threonine-protein kinase PLK4, Serine/threonine-protein kinase Sak, STK18	Homo sapiens

WikiGenes	edit this page new
UniProt	O00444, Q15455, B7Z8G7
IntAct	O00444
PDB Structure	3COK
OMIM	605031
NCBI Gene	10733
NCBI RefSeq	NP_001177726, NP_055079
NCBI RefSeq	NM_014264, NM_001190561
NCBI UniGene	10733
NCBI Accession	Y13115, Z25433

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Collectively, our results suggest that CUL1 may **function** as a tumor suppressor by **regulating** PLK4 protein levels and thereby restraining excessive daughter centriole formation at maternal centrioles. [2009]

Plk4 trans-autophosphorylation **regulates** centriole number by controlling betaTrCP-mediated degradation. [2010]

Cep152 **interacts** with Plk4 [?] and is required for centriole duplication. [2010]

Cep152 can be **phosphorylated** by Plk4 [?] in vitro, suggesting that Cep152 acts with Plk4 [?] to initiate centriole formation. [2010]

Cullin 1 **functions** as a centrosomal suppressor of centriole multiplication by **regulating** polo-like kinase 4 protein levels. [2009]

Furthermore, our results imply that Plk2 **mediated** centriole duplication is dependent on Plk4 function. [2008]

Overexpression of a Plk4-**binding**-deficient mutant of Asl prevented centriole duplication in cultured cells and embryos. [2010]

Interfering with Cep152 **function** prevents recruitment of Plk4 to the centrosome and **promotes** loss of CPAP, a protein required for the control of centriole length in Plk4-regulated centriole biogenesis. [2010]

Our results suggest that Cep152 **recruits** Plk4 and CPAP to the centrosome to ensure a faithful centrosome duplication process. [2010]

In this study, we show in human and frog cells that Plk4 [?] **interacts** with the centrosome protein Cep152, the orthologue of Drosophila melanogaster Asterless. [2010]

Thus, SAK repression by p53 is likely **mediated** through the recruitment of HDAC repressors, and SAK repression contributes to p53-induced apoptosis. [2005]

We conclude that active Plk4 **promotes** its own degradation by catalyzing betaTrCP binding through trans-autophosphorylation (phosphorylation by the other kinase in the dimer) within homodimers. [2010]

Significantly, p53-**mediated** SAK repression was largely reversed in a dose-dependent manner by Trichostatin A [?], a potent histone deacetylase (HDAC) inhibitor, suggesting an involvement of HDAC transcription repressors in SAK repression by p53. [2005]

CONCLUSIONS: SAK [?]/PLK4 [?] is necessary for centriole duplication both in Drosophila and human cells. [2005]

Concept & Implementation: by Robert Hoffmann

While significant advances have been made in understanding how PLK4 is regulated it is certain that additional regulatory mechanisms exist to safeguard the fidelity of centriole duplication. [2010]

PLK4 is required for centriole duplication and strongly stimulates centriole multiplication when aberrantly expressed. [2009]

We found that this activity of CUL1 involves the degradation of Polo-like kinase 4 (PLK4) at maternal centrioles. [2009]

The Polo kinase Plk4 functions in centriole duplication. [2005]

Here, we identify Plk4 as a key regulator of centriole duplication. [2005]

Finally, we show that depletion of SAK [?] in human cells also prevents centriole duplication and gives rise to mitotic abnormalities. [2005]

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Unexpectedly, we found that stable overexpression of kinase-dead Plk4 leads to centriole overduplication. [2010]

Our data indicate that centriole overduplication results from disruption of Plk4 trans-autophosphorylation by kinase-dead Plk4, which then shields endogenous Plk4 from recognition by betaTrCP. [2010]

Autophosphorylation of polo-like kinase 4 and its role in centriole duplication. [2010]

Polo-like kinase 4 (PLK4) is a key regulator of this process whose kinase activity is essential for centriole duplication. [2010]

Depletion of Cep152 prevents both normal centriole duplication and Plk4 [?]-induced centriole amplification and results in a failure to localize Sas6 to the centriole, an early step in duplication. [2010]

Overexpression of Cep152 (1-217) mislocalizes Plk4 [?], but both Cep152 and Plk4 [?] are able to localize to the centriole independently of the other. [2010]

Our findings identify independent functions for Asl as a scaffold for Plk4 and Sas-4 that facilitates self-assembly and duplication of the centriole and organization of pericentriolar material. [2010]

Centriole assembly and duplication is controlled by Polo-like-kinase 4 (Plk4): these processes fail if Plk4 is downregulated and are promoted by Plk4 overexpression. [2010]

These data suggest that PLK4 activity is restricted to the centrosome to prevent aberrant centriole assembly and sustained kinase activity is required for centriole duplication. [2010]

Recent data have also shown that active PLK4 is restricted to the centrosome, a mechanism that could serve to prevent aberrant centriole assembly elsewhere in the cell. [2010]

We show that overexpression of Polo-like kinase 4 (Plk4) in human cells induces centrosome amplification through the simultaneous generation of multiple procentrioles adjoining each parental centriole. [2007]

Plk4-induced centriole biogenesis in human cells. [2007]

The centriolar protein Polo-like kinase 4 (Plk4) is a key regulator of centriole biogenesis and is crucial for maintaining constant centriole number, but the mechanisms regulating its activity and expression are only beginning to emerge. [2010]

Gamma-tubulin-containing abnormal centrioles are induced by insufficient Plk4 in human HCT116 colorectal cancer cells. [2009]

In this study, we show that the pericentriolar material protein, Cep152, interacts with the distinctive cryptic Polo-box of Plk4 via its N-terminal domain and is required for Plk4-induced centriole overduplication. [2010]

Activation of PLK4 at the replicating daughter centriole is delayed until G2, but a level equivalent to the replicating mother centriole is achieved in S phase. [2010]

Autophosphorylation probably plays a role in the process of centriole duplication, because mimicking S305 phosphorylation enhances the ability of overexpressed PLK4 to induce centriole amplification. [2010]

Cep152 and Plk4 [?] colocalize at the centriole throughout the cell cycle. [2010]

SAK [?]/PLK4 [?] is required for centriole duplication and flagella development. [2005]

These results suggest that HCT116 cells fail to organize the ninefold symmetry of centrioles due to insufficient Plk4. [2009]

top

Plk4, a mammalian homolog of ZYG-1 essential for initiation of centriole biogenesis, is not associated with the gamma-tubulin-specific abnormal centrosomes. [2009]

Both gain and loss of function studies have identified the Polo-like kinase Plk4/Sak as a crucial regulator of centriole biogenesis, but the mechanisms governing centrosome duplication are incompletely understood. [2010]

RESULTS: Here, we show that downregulation of SAK [?] in Drosophila cells, by mutation or RNAi, leads to loss of centrioles, the core structures of centrosomes. [2005]

Centrioles duplicate once per cell cycle, and duplication requires Plk4 [?], a member of the Polo-like kinase family; however, the mechanism linking Plk4 [?] activity and centriole formation is unknown. [2010]

Active PLK4 is detectable on the replicating mother centriole in G1/S [?], with the proportion of active kinase increasing through interphase to reach a maximum in mitosis. [2010]

The majority of spermatids in SAK [?] mutants lack centrioles and so are unable to make sperm axonemes. [2005]

We also show that SAK [?] mutants lose their centrioles during the mitotic divisions preceding male meiosis but still produce cysts of 16 primary spermatocytes as in the wild-type. [2005]

Importantly, we show that S305-phosphorylated PLK4 is specifically sequestered at the centrosome contrary to the nonphosphorylated form. [2010]

The amount of Plk4 at each centrosome was less in cells with abnormal centrosomes than cells without gamma-tubulin-specific abnormal centrosomes. [2009]

Cep152 acts as a scaffold for recruitment of Plk4 and CPAP to the centrosome. [2010]

Both gain- and loss-of-function experiments demonstrate that Plk4 is required--in cooperation with Cdk2, CP110 and Hs-SAS6--for the precise reproduction of centrosomes during the cell cycle. [2005]

Comparative expression of the mitotic regulators SAK and PLK in colorectal cancer. [2001]

CONCLUSIONS: The polo family mitotic regulators SAK and PLK are both aberrantly expressed in colorectal cancer. [2001]

The potential prognostic significance of SAK and PLK expression in colorectal cancer will be evaluated in the future. [2001]

METHODS: In this study, SAK expression was evaluated in a series of sporadic human colorectal cancer specimens (n = 74) and compared with that of PLK. [2001]

The interaction requires the N-terminal 217 residues of Cep152 and the crypto Polo-box of Plk4 [?]. [2010]

Here we show that the centriolar protein Asterless (Asl; human orthologue CEP152) provides a conserved molecular platform, the amino terminus of which interacts with the cryptic Polo box of Plk4 whereas the carboxy terminus interacts with the centriolar protein Sas-4 (CPAP in humans). [2010]

Here, we show that PLK4 autophosphorylation of serine S305 is a consequence of kinase activation and enables the active fraction to be identified in the cell. [2010]

Human cells depleted of SAK [?] show error-prone mitosis, likely to underlie its tumor-suppressor role. [2005]

SAK, a new polo-like kinase, is transcriptionally repressed by p53 and induces apoptosis upon RNAi silencing. [2005]

top

These findings provide an attractive explanation for the crucial function of Plk4 in cell proliferation and have implications for the role of Polo kinases in tumorigenesis. [2005]

Plk4 is the most structurally divergent Polo family member; it is maximally expressed in actively dividing tissues and is essential for mouse embryonic development. [2005]

SAK [?] -/- mice die during embryogenesis, whereas SAK [?] +/- mice develop liver and lung tumors and SAK [?] +/- MEFs show mitotic abnormalities. [2005]

Transcriptional analysis with luciferase reporters driven by SAK promoter deletion fragments identified SP-1 and CREB binding sites, which together conferred a two-fold SAK repression by p53. [2005]

Biologically, SAK RNA interference (RNAi) silencing induced apoptosis, whereas SAK overexpression attenuated p53-induced apoptosis. [2005]

Computer search of a 1.7-kb SAK promoter sequence revealed three putative p53 binding sites, but p53 failed to bind to any of these sites, indicating that SAK repression by p53 was not through a direct p53 binding to the promoter. [2005]

Little has been, therefore, elucidated how Sak is regulated and how Sak contributes to cell proliferation. [2001]

SAK, a polo family member with unique properties, had not been systematically studied in any tumor type. [2001]

SAK and PLK are members of the polo family of serine [?] threonine [?] kinases, which in lower organisms have been shown to be required for the precise regulation of mitosis. [2001]

Functional validation using siRNA knockdown in multiple tumor cell lines showed that C13orf34, MAD2L1, PLK4, TPD52, and DEPDC1B each significantly altered radiation sensitivity in at least two cancer cell lines. [2010]

This is achieved, in part, by an autoregulatory mechanism, whereby PLK4 autophosphorylates residues in a PEST sequence located carboxy-terminal to its catalytic domain. [2010]

We found that CUL1 is critical for the degradation of active PLK4 following deregulation of cyclin E/cyclin-dependent kinase 2 activity, as is frequently observed in human cancer cells, as well as for baseline PLK4 protein stability. [2009]

In addition, the formation of abnormal structures was abolished by expression of exogenous Plk4, but not SAS6 and Cep135/Bld10p, which are downstream regulators required for the organization of nine-triplet microtubules. [2009]

Sak serine-threonine kinase acts as an effector of Tec tyrosine [?] kinase. [2001]

RESULTS: In the majority of cases, both SAK and PLK were more highly expressed in tumor tissue than in adjacent normal intestinal mucosa. [2001]

Levels of SAK and PLK expression in tumor relative to paired normal mucosa correlated directly with patient age and with each other but did not correlate with tumor stage. [2001]

This phenotype depends on the presence of endogenous wild-type Plk4. [2010]

Plk4 [?] (+/-) murine embryonic fibroblasts (MEFs) at early passage show a high incidence of multinucleation, supernumerary centrosomes, and a near-tetraploid karyotype. [2010]

Sak [?] transcripts are present in S/G2/M phase cells, and in proliferating cell layers of the mouse embryo and adult tissues. [2000]

The Sak [?] gene encodes a serine [?]/threonine [?] kinase, which is a member of the Polo family of mitotic regulators. [2000]

top

Primer extension analysis of murine Sak [?] revealed one major transcription start site at position -303bp relative to the start of translation. [2000]

Using various Sak [?] promoter/luciferase constructs, the core promoter region required for expression was located within 400bp of the message Cap site, and sequence further 5' strongly suppressed transcription. [2000]

The murine Sak [?] gene is located on the proximal arm of mouse chromosome 13, as determined by RFLP analysis. [2000]

Plk4 [?] is required for cytokinesis and maintenance of chromosomal stability. [2010]

Here we show that loss of heterozygosity (LOH) occurs at the Plk4 [?] locus in 50% of human hepatocellular carcinomas (HCC) and is present even in preneoplastic cirrhotic liver nodules. [2010]

Our results indicate that haploid levels of Plk4 [?] disrupt RhoGTPase function during cytokinesis, resulting in aneuploidy and tumorigenesis, thus implicating early LOH at Plk4 [?] as one of the drivers of human hepatocellular carcinogenesis. [2010]

However when these cells commit to differentiate into trophoblast giant (TG) cells, Hand1 is **phosphorylated** by the polo-like kinase Plk4 (Sak) and released into the nucleus to activate downstream target genes. [2008]

In Drosophila, centrioles are not necessary for somatic cell divisions.(9,10) However, we show here that mitotic abnormalities arise in syncytial SAK/PLK4-derived mutant embryos resulting in lethality. [2008]

Polo-like kinase 4 [?] (Plk4 [?]) regulates both modes of centriole biogenesis, and Plk4 [?] deregulation has been linked to tumor development [1, 3]. [2011]

The conserved protein kinase Polo-like kinase 4 [?] (Plk4) has a key role in controlling centriole biogenesis. [2010]

ABSTRACT: Polo-like kinase 4 (PLK4) is a unique member of the Polo-like family of kinases that shares little homology with its siblings and has an essential role in centriole duplication. [2010]

We show that Plx4, the Xenopus homolog of mammalian Plk4 [?] and Drosophila Sak [?], induces de novo centriole formation in••vivo in activated oocytes and in egg extracts, but not in immature or in••vitro matured oocytes. [2011]

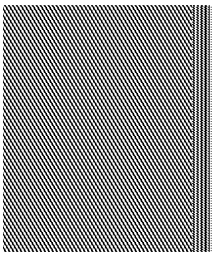
Moreover male meiosis fails in both SAK/PLK4 and DSAS-4 mutant spermatids that have no centrioles. [2008]

Here, we show that expression of stabilized mutant beta-catenin, which mimics mutations found in cancer, results in extra non-microtubule nucleating structures that contain a subset of centrosome proteins including gamma-tubulin and centrin, but not polo-like kinase 4 [?] (Plk4 [?]), SAS-6 or pericentrin. [2010]

One of these SSAPs was identified as Sak and was found in the virulent L. lactis phage ul36, which belongs to the Siphoviridae family [4, 5]. [2008]

In Staphylococcus aureus phages encoding immune evasion molecules (SAK, SCIN, CHIPS), which integrate specifically into the beta-haemolysin (Hlb) gene, are widely distributed. [2006]

The predicted protein sequences of Rab7a and Rab7b contain all characteristic domains essential for Rab function: the effector domain (YRATVGADF) and four GTP-binding consensus sequences (GDSGVGKT, WDTAGQ, NKLD, SAK) as well as the prenylation motif (-CC) at the C-terminus indispensable for Rab binding to the membrane. [2006]



Sea anemones have proven to be a rich source of pharmacological tools, and some of the SAK toxins are now useful drugs for the diagnosis and treatment of autoimmune diseases. [2009]

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